=> d his

(FILE 'HOME' ENTERED AT 09:05:35 ON 17 NOV 2002)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
09:06:01 ON 17 NOV 2002
L1 18424 S (BOTULINUM TOXIN) OR (BUTYRICUM TOXIN) OR (TETANI TOXIN) OR (
L2 49279 S GNRH
L3 4813 S GNRH RECEPTOR
L4 2836 S (TARGET? MOIETY) OR (TARGET? DOMAIN) OR (TARGET? COMPONENT)
L5 0 S L1 (P) L2
L6 0 S L1 (P) L3
L7 8 S L1 (P) L4
L8 4 DUPLICATE REMOVE L7 (4 DUPLICATES REMOVED)
L9 88206 S LIGHT CHAIN
L10 673 S (TRANSLOCAT? DOMAIN) OR (TRANSLOCAT? COMPONENT)
L11 0 S L9 (P) L10 (P) L4
L12 9 S L9 (P) L4
L13 0 S L12 (P) L1
L14 5 DUPLICATE REMOVE L12 (4 DUPLICATES REMOVED)
L15 5 S L14 NOT L8
L16 1 S GONADOTROPHIN RELATED DISEASE
L17 472293 S (BREAST CANCER) OR (PROSTATE CANCER) OR (PANCREATIC CANCER) O
L18 0 S (L16 OR L17) (P) (L8 OR L14)

=> log y

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FILE 'HOME' ENTERED AT 09:05:35 ON 17 NOV 2002

=> file medline caplus biosis embase scisearch agricola
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'MEDLINE' ENTERED AT 09:06:01 ON 17 NOV 2002

FILE 'CAPLUS' ENTERED AT 09:06:01 ON 17 NOV 2002
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FILE 'BIOSIS' ENTERED AT 09:06:01 ON 17 NOV 2002
COPYRIGHT (C) 2002 BIOLOGICAL ABSTRACTS INC.(R)

FILE 'EMBASE' ENTERED AT 09:06:01 ON 17 NOV 2002
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FILE 'SCISEARCH' ENTERED AT 09:06:01 ON 17 NOV 2002
COPYRIGHT (C) 2002 Institute for Scientific Information (ISI) (R)

FILE 'AGRICOLA' ENTERED AT 09:06:01 ON 17 NOV 2002

=> s (botulinum toxin) or (butyricum toxin) or (tetani toxin) or (clostridial toxin)
L1       18424 (BOTULINUM TOXIN) OR (BUTYRICUM TOXIN) OR (TETANI TOXIN) OR
               (CLOSTRIDIAL TOXIN)

=> s gnrh
L2       49279 GNRH

=> s gnrh receptor
L3        4813 GNRH RECEPTOR

=> s (target? moiety) or (target? domain) or (target? component)
L4        2836 (TARGET? MOIETY) OR (TARGET? DOMAIN) OR (TARGET? COMPONENT)

=> s l1 (p) l2
L5           0 L1 (P) L2

=> s l1 (p) l3
L6           0 L1 (P) L3

=> s l1 (p) l4
L7           8 L1 (P) L4

=> duplicate remove l7
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L7
L8            4 DUPLICATE REMOVE L7 (4 DUPLICATES REMOVED)

=> d l8 1-4 ibib abs

L8   ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:         2002:89857  CAPLUS
DOCUMENT NUMBER:          136:145260
TITLE:                    Clostridial toxin derivatives and methods for treating
                          pain
INVENTOR(S):              Donovan, Stephen
PATENT ASSIGNEE(S):       Allergan Sales, Inc., USA
SOURCE:                   PCT Int. Appl., 67 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   3
PATENT INFORMATION:

     PATENT NO.       KIND  DATE           APPLICATION NO.  DATE
```

WO 2002007759	A2	20[redacted]131	WO 2001-US21984	2001[redacted]12	

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-625098 A 20000725

AB Methods for treating a bone tumor, in particular pain assocd. with bone tumor, by administration to a patient of a therapeutically effective amt. of an agent are disclosed. The agent may include a clostridial neurotoxin component attached to a targeting moiety, wherein the targeting moiety is selected from the group consisting of transmission compds. which can be released from neurons upon the transmission of pain signals by the neurons, and compds. substantially similar to the transmission compds.

L8 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:241331 CAPLUS
DOCUMENT NUMBER: 136:273210
TITLE: Clostridial toxin derivatives and methods for treating pain
INVENTOR(S): Donovan, Stephen
PATENT ASSIGNEE(S): Allergan Sales, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 20 pp., Cont.-in-part of U.S. Ser. No. 625,098.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002037833	A1	20020328	US 2001-922093	20010803

PRIORITY APPLN. INFO.: US 2000-489667 A2 20000119
US 2000-625098 A2 20000725

AB Agents for treating pain, methods for producing the agents and methods for treating pain by administration to a patient of a therapeutically effective amt. of the agent are disclosed. The agent can include a clostridial neurotoxin, or a component or fragment or deriv. thereof, attached to a ***targeting*** ***moiety*** , wherein the ***targeting*** ***moiety*** is selected from a group consisting of transmission compds. which can be released from neurons upon the transmission of pain signals by the neurons, and compds. substantially similar to the transmission compds. The agent comprises a ***botulinum*** ***toxin*** component covalently coupled to substance P.

L8 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:228744 CAPLUS
DOCUMENT NUMBER: 134:247267
TITLE: Clostridial neurotoxin targeted conjugates for inhibition of secretion from non-neuronal cells
INVENTOR(S): Foster, Keith Alan; Chaddock, John Andrew; Purkiss, John Robert; Quinn, Conrad Padraig
PATENT ASSIGNEE(S): Microbiological Research Authority, UK
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001021213	A2	20010329	WO 2000-GB3669	20000925
WO 2001021213	A3	20020711		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU,
ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
EP 1235594 A2 20020904 EP 2000-962721 20000925
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL
PRIORITY APPLN. INFO.: GB 1999-22554 A 19990923
WO 2000-GB3669 W 20000925

AB A method of treatment of disease by inhibition of cellular secretory processes is provided. The method has particular application in the treatment of diseases dependent on the exocytotic activity of endocrine cells, exocrine cells, inflammatory cells, cells of the immune system, cells of the cardiovascular system, and bone cells. Agents and compns. therefor, as well as methods for manufg. these agents and compns., are provided. In a preferred embodiment a clostridial neurotoxin, substantially devoid of holotoxin binding affinity for neuronal cells of the presynaptic muscular junction, is assocd. with a ***targeting*** ***moiety*** . The ***targeting*** ***moiety*** is selected such that the ***clostridial*** ***toxin*** conjugate so formed may be directed to a non-neuronal target cell to which the conjugate may bind. Following binding, a neurotoxin component of the conjugate, which is capable of inhibition of cellular secretion, passes into the cytosol of the target cell by cellular internalization mechanisms. Thereafter, inhibition of secretion from the target cell is effected.

L8 ANSWER 4 OF 4 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2000273725 MEDLINE
DOCUMENT NUMBER: 20273725 PubMed ID: 10813652
TITLE: Identification of novel small molecule ligands that bind to tetanus toxin.
AUTHOR: Lightstone F C; Prieto M C; Singh A K; Piqueras M C; Whittal R M; Knapp M S; Balhorn R; Roe D C
CORPORATE SOURCE: Biology and Biotechnology Research Program, Lawrence Livermore National Laboratory, Livermore, California 94550, USA.
CONTRACT NUMBER: RR01614 (NCRR)
SOURCE: CHEMICAL RESEARCH IN TOXICOLOGY, (2000 May) 13 (5) 356-62. Journal code: 8807448. ISSN: 0893-228X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200007
ENTRY DATE: Entered STN: 20000720
Last Updated on STN: 20000720
Entered Medline: 20000711

AB Tetanus toxin belongs to a family of clostridial protein neurotoxins for which there are no known antidotes. Another closely related member of this family, ***botulinum*** ***toxin*** , is being used with increasing frequency by physicians to treat severe muscle disorders. ***Botulinum*** ***toxin*** has also been produced in large quantities by terrorists for use as a biological weapon. To identify small molecule ligands that might bind to the ***targeting*** ***domain*** of tetanus and ***botulinum*** ***toxins*** and to facilitate the design of inhibitors and new reagents for their detection, molecular docking calculations were used to screen a large database of compounds for their potential to bind to the C fragment of tetanus toxin. Eleven of the predicted ligands were assayed by electrospray ionization mass spectrometry (ESI-MS) for binding to the tetanus toxin C fragment, and five ligands (45%) were found to bind to the protein. One of these compounds, doxorubicin, was observed to have strong hydrophobic interactions with the C fragment. To check the ligands for their ability to compete with ganglioside binding, each was also tested using a GT1b liposome assay. Doxorubicin was the only ligand found to competitively bind the tetanus toxin C fragment with an appreciable binding constant (9.4 microM).

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=> d his

     (FILE 'HOME' ENTERED AT 09:05:35 ON 17 NOV 2002)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     09:06:01 ON 17 NOV 2002
L1         18424 S (BOTULINUM TOXIN) OR (BUTYRICUM TOXIN) OR (TETANI TOXIN) OR (
L2         49279 S GNRH
L3          4813 S GNRH RECEPTOR
L4          2836 S (TARGET? MOIETY) OR (TARGET? DOMAIN) OR (TARGET? COMPONENT)
L5             0 S L1 (P) L2
L6             0 S L1 (P) L3
L7             8 S L1 (P) L4
L8             4 DUPLICATE REMOVE L7 (4 DUPLICATES REMOVED)

=> s light chain
L9        88206 LIGHT CHAIN

=> s (translocat? domain) or (translocat? component)
L10         673 (TRANSLOCAT? DOMAIN) OR (TRANSLOCAT? COMPONENT)

=> s l9 (p) l10 (p) l4
L11           0 L9 (P) L10 (P) L4

=> s l9 (p) l4
L12           9 L9 (P) L4

=> s l12 (p) l1
L13           0 L12 (P) L1

=> duplicate remove l12
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L12
L14            5 DUPLICATE REMOVE L12 (4 DUPLICATES REMOVED)

=> s l14 not l8
L15           5 L14 NOT L8

=> d l15 1-5 ibib abs

L15  ANSWER 1 OF 5     MEDLINE
ACCESSION NUMBER:    2002136343     MEDLINE
DOCUMENT NUMBER:     21840684   PubMed ID: 11851407
TITLE:               Dissection of the pathway of molecular recognition by
                     calmodulin.
AUTHOR:              Kranz James K; Flynn Peter F; Fuentes Ernesto J; Wand A
                     Joshua
CORPORATE SOURCE:    The Johnson Research Foundation and Department of
                     Biochemistry and Biophysics, University of Pennsylvania,
                     Philadelphia, Pennsylvania 19104-6059, USA.
CONTRACT NUMBER:     DK39806 (NIDDK)
     GM20206 (NIGMS)
SOURCE:              BIOCHEMISTRY, (2002 Feb 26) 41 (8) 2599-608.
                     Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY:        United States
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         200203
ENTRY DATE:          Entered STN: 20020302
                     Last Updated on STN: 20020403
                     Entered Medline: 20020328
AB   Amide hydrogen exchange has been used to examine the structural dynamics
     and energetics of the interaction of a peptide corresponding to the
     calmodulin-binding domain of smooth muscle myosin   ***light***
       ***chain***   kinase (smMLCKp) with calcium-saturated calmodulin.
     Heteronuclear NMR (15)N-(1)H correlation spectroscopy was used to quantify
     amide proton exchange rates of the uniformly (15)N-labeled domain bound to
     calmodulin. A key feature of a proposed model for molecular recognition by
     calmodulin [Ehrhardt et al. (1995) Biochemistry 34, 2731-2738] is tested
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by examination of the dependence of amide hydrogen exchange on applied hydrostatic pressure. Hydrogen exchange rates and corresponding protection factors (1/K(op)) for individual amide protons of the bound smMLCKp domain span 5 orders of magnitude at ambient pressure. Individual protection factors decrease significantly in a linear fashion with increasing hydrostatic pressure. A common pressure dependence is revealed by a constant large negative volume change across the residues comprising the core of the bound helical domain. The pattern of protection factors and their response to hydrostatic pressure is consistent with a structural reorganization that results in the concerted disruption of ion pairs between calmodulin and the bound domain. These observations reinforce a model for the molecular recognition pathway where formation of the initial encounter complex is followed by helix-coil transitions in the bound state and subsequent concerted formation of the extensive ion pair network defining the intermolecular contact surface between CaM and the ***target*** ***domain*** in the final, compact complex structure.

L15 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:208290 CAPLUS
DOCUMENT NUMBER: 134:247944
TITLE: Methods used for production of subunit optimized fusion proteins, use of immunoglobulin chains
INVENTOR(S): Pollock, Dan; Meade, Harry M.; Bosslet, Klaus
PATENT ASSIGNEE(S): Genzyme Transgenics Corporation, USA
SOURCE: PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001019842	A1	20010322	WO 2000-US25558	20000918
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2000014524	A	20020611	BR 2000-14524	20000918
EP 1237900	A1	20020911	EP 2000-963585	20000918
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
NO 2002001244	A	20020513	NO 2002-1244	20020313

PRIORITY APPLN. INFO.: US 1999-399079 A2 19990917
WO 2000-US25558 W 20000918

AB The invention provides a method for making fusion proteins which involves having a ***target*** ***moiety*** , such as an Ig subunit, fused to a second member, such as a multimeric enzyme. The ***targeting*** ***moiety*** (Ig) and second member (enzyme) of the fusion protein are chosen such that the fusion protein assemblies into a complex having the no. of subunits which optimizes the activity of the multimeric form of the enzyme. The invention relates that the Ig subunit is modified. The invention specifically provides for the methods used for fusing an anti-carcinoembryonic antigen human Ig ***light*** ***chain*** to a human Ig heavy chain-.beta.-glucuronidase fusion protein. The Ig heavy chain-.beta.-glucuronidase assemblies with the Ig ***light*** ***chain*** to produce a functional complex with .beta.-glucuronidase activity. The invention also provides DNA constructs (plasmids) used in transforming mammals for prodn. of said fusion proteins which include: (1) a single DNA construct contg. sequences encoding both the Ig ***light*** ***chain*** and Ig heavy chain-.beta.-glucuronidase fusion protein; (2) DNA construct contg. sequences encoding the Ig ***light*** ***chain*** ; and (3) DNA construct contg. sequences encoding the Ig heavy chain-.beta.-glucuronidase fusion protein. The invention further provides that the fusion protein can be produced in milk of transgenic mammals, if the DNA construct used to transform said mammal contains: (1) an insulator sequence (control element); (2) a signal sequence (either

from Ig or .beta. casein), and (3) promoter and 3'-untranslated sequences from the .beta. casein ge[redacted] In the example section, the i[redacted]ention described in detail the materials and methods used in prodn. of said DNA constructs and fusion protein, and characterized transgenic mice transformed with said DNA constructs. The invention also provided the DNA and amino acid sequences of the anti-carcinoembryonic antigen light and heavy Ig chains, and sequence changes due to modifications.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:96139 CAPLUS
DOCUMENT NUMBER: 130:167161
TITLE: Directed cytolysis of target cells, agents and compositions causing cytolysis, and compounds that can be used to produce the agents
INVENTOR(S): Soegaard, Morten; Abrahmsen, Lars; Lando, Peter; Forsberg, Goran; Kalland, Terje; Dohlsten, Mikael
PATENT ASSIGNEE(S): Pharmacia & Upjohn Ab, Swed.
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9904820	A2	19990204	WO 1998-EP4219	19980702
WO 9904820	A3	19990812		
W: AU, BG, BR, CA, CN, CZ, HU, ID, IL, JP, KR, MX, NO, NZ, PL, RO, SG, SI, UA, US, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9884415	A1	19990216	AU 1998-84415	19980702
AU 748097	B2	20020530		
EP 998305	A2	20000510	EP 1998-935025	19980702
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI				
BR 9815493	A	20001031	BR 1998-15493	19980702
JP 2001510687	T2	20010807	JP 2000-503871	19980702
ZA 9806431	A	19990127	ZA 1998-6431	19980720
NO 2000000265	A	20000315	NO 2000-265	20000119

PRIORITY APPLN. INFO.:			
US 1997-53211P	P	19970721	
SE 1997-4170	A	19971114	
WO 1998-EP4219	W	19980702	

AB A method for inactivating target cells in the presence of T cells by bringing the two types of cells in contact with a superantigen (SAg) in the presence of an immune modulator, characterized in that at least one of the superantigen and the immune modulator is in the form of a conjugate between a "free" superantigen (SAg) and a moiety targeting the conjugate to the target cells. A superantigen conjugate complying with the formula (I): (T)x(SAg)y(IM)z; (a) T is a targeting moiety, SAg corresponds to a free superantigen, IM is an immune modulator that is not a superantigen and T, SAg and IM are linked together via org. linkers B; (b) x, y and z are integers that typically are selected among 0-10 and represent the no. of moieties T, SAg and IM, resp., in a given conjugate mol., with the provision that y > 0 and also one or both of x and z > 0. The superantigen conjugate is preferably a triple fusion protein. A targeted immune modulator, characterized in that it is a conjugate between a targeting moiety (T''') and a modified immune modulator (IM'''). The conjugate complies with a formula analogous to formula (I) except for the imperative presence of the modified immune modulator. A superantigen moiety may be present. A DNA mol. encoding a superantigen and an immune modulator. Thus, triple fusion proteins contg. CD80 or interleukin 2, anti-C215 antigen Fab, and Staphylococcal enterotoxin A were prepd. and used for tumor therapy.

L15 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:761969 CAPLUS
DOCUMENT NUMBER: 130:29189
TITLE: Fusion proteins of prodrug activating enzymes and

targetting moieties and their therapeutic uses
INVENTOR(S): Emery [redacted]tephen Charles; Blakey, David C[redacted]rles
PATENT ASSIGNEE(S): Zeneca Limited, UK
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9851787	A2	19981119	WO 1998-GB1294	19980505
WO 9851787	A3	19990401		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9872254	A1	19981208	AU 1998-72254	19980505
AU 734915	B2	20010628		
GB 2338484	A1	19991222	GB 1999-22815	19980505
GB 2338484	B2	20011107		
EP 979292	A2	20000216	EP 1998-919380	19980505
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
BR 9808769	A	20000801	BR 1998-8769	19980505
JP 2001526539	T2	20011218	JP 1998-548892	19980505
ZA 9803931	A	19981110	ZA 1998-3931	19980508
NO 9905475	A	20000107	NO 1999-5475	19991109
US 6339070	B1	20020115	US 1999-423439	19991109

PRIORITY APPLN. INFO.: GB 1997-9421 A 19970510
WO 1998-GB1294 W 19980505

AB A method of limiting prodrug activation to a specific cell type by targetting prodrug activating enzymes to that cell type as fusion proteins with cell-specific ligands is described. The cell-specific ligand may be an antibody, e.g. to a disease marker. Alternatively, the gene for the protein may be placed under control of a promoter that is only functional in the disease, e.g. a tumor marker gene. Chimeric genes for fusion proteins of carboxypeptidase G2 (CPG2) and heavy and light chains of antibodies to carcinoembryonic antigen were constructed by std. methods. The fusion protein manufd. in animal cells dimerized through the dimerization domain of CPG2. The fusion protein was able to activate the prodrug PGP to the cytotoxic 4-[N,N-Bis(2-chloroethyl)amino]phenol. HCT116 cells transformed with the gene for this protein had an IC50 for PGP of 200 .mu.M compared to 1 .mu.M for the activated drug.

L15 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:575 CAPLUS
DOCUMENT NUMBER: 120:575
TITLE: Immunotoxins directed against c-erbB-2-related surface antigens
INVENTOR(S): Rosenblum, Michael G.; Shawver, Laura K.
PATENT ASSIGNEE(S): Research Development Foundation, USA
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9321232	A1	19931028	WO 1993-US3292	19930408
W: AU, CA, FI, JP, KR, NO, NZ, RU				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
ZA 9302522	A	19931220	ZA 1993-2522	19930101
AU 9342804	A1	19931118	AU 1993-42804	19930408
AU 671642	B2	19960905		

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     EP 635030         A1   19950125       EP 1993-912147   19930408
        R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE
     JP 07505882       T2   19950629       JP 1993-518465   19930408
     RU 2130780        C1   19990527       RU 1994-45908    19930408
     IL 105345         A1   20000928       IL 1993-105345   19930408
     NO 9403777        A    19941129       NO 1994-3777     19941007
     FI 9404731        A    19941202       FI 1994-4731     19941007
PRIORITY APPLN. INFO.:                   US 1992-867728   A  19920410
                                         WO 1993-US3292   A  19930408
AB   The novel immunotoxins comprise a c-erbB-2   ***targeting***
       ***moiety***   (e.g., a segment, a   ***light***     ***chain***   , or a
     heavy chain of an antibody to c-erbB-2) and a cell growth modulator (e.g.,
     a plant toxin such as gelonin).  The immunotoxins kill neoplastic cells
     overexpressing c-erbB-2 protein and therefore are useful for treating
     mammary, human ovarian, lung, and gastric carcinomas; salivary gland and
     colon adenocarcinomas; and bone marrow leukemia.  Thus, gelonin was
     purified from seeds of Gelonium multiflorum, and mouse monoclonal antibody
     to c-erbB-2 was prepd.  SPDP-modified monoclonal antibody was conjugated
     with 2-iminothiolane-modified gelonin.  The cytotoxicity of the
     antibody-gelonin conjugates was demonstrated on human breast
     adenocarcinoma cells.


=> d his

     (FILE 'HOME' ENTERED AT 09:05:35 ON 17 NOV 2002)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     09:06:01 ON 17 NOV 2002
L1         18424 S (BOTULINUM TOXIN) OR (BUTYRICUM TOXIN) OR (TETANI TOXIN) OR (
L2         49279 S GNRH
L3          4813 S GNRH RECEPTOR
L4          2836 S (TARGET? MOIETY) OR (TARGET? DOMAIN) OR (TARGET? COMPONENT)
L5             0 S L1 (P) L2
L6             0 S L1 (P) L3
L7             8 S L1 (P) L4
L8             4 DUPLICATE REMOVE L7 (4 DUPLICATES REMOVED)
L9         88206 S LIGHT CHAIN
L10          673 S (TRANSLOCAT? DOMAIN) OR (TRANSLOCAT? COMPONENT)
L11            0 S L9 (P) L10 (P) L4
L12            9 S L9 (P) L4
L13            0 S L12 (P) L1
L14            5 DUPLICATE REMOVE L12 (4 DUPLICATES REMOVED)
L15            5 S L14 NOT L8

=> s gonadotrophin related disease
L16            1 GONADOTROPHIN RELATED DISEASE

=> s (breast cancer) or (prostate cancer) or (pancreatic cancer) or (endometrial cancer)
L17       472293 (BREAST CANCER) OR (PROSTATE CANCER) OR (PANCREATIC CANCER) OR
                 (ENDOMETRIAL CANCER)

=> s (l16 or l17) (p) (l8 or l14)
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L115) (P) '
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L116) (P) '
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L117) (P) '
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L118) (P) '
L18            0 (L16 OR L17) (P) (L8 OR L14)

=> d his

     (FILE 'HOME' ENTERED AT 09:05:35 ON 17 NOV 2002)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     09:06:01 ON 17 NOV 2002
L1         18424 S (BOTULINUM TOXIN) OR (BUTYRICUM TOXIN) OR (TETANI TOXIN) OR (
L2         49279 S GNRH
L3          4813 S GNRH RECEPTOR
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L4          2836 S (TARGET? MOIETY) OR (TARGET? DOMAIN) OR (TARGET? COMPONENT)
L5             0 S L1 (P) L2
L6             0 S L1 (P) L3
L7             8 S L1 (P) L4
L8             4 DUPLICATE REMOVE L7 (4 DUPLICATES REMOVED)
L9         88206 S LIGHT CHAIN
L10          673 S (TRANSLOCAT? DOMAIN) OR (TRANSLOCAT? COMPONENT)
L11            0 S L9 (P) L10 (P) L4
L12            9 S L9 (P) L4
L13            0 S L12 (P) L1
L14            5 DUPLICATE REMOVE L12 (4 DUPLICATES REMOVED)
L15            5 S L14 NOT L8
L16            1 S GONADOTROPHIN RELATED DISEASE
L17       472293 S (BREAST CANCER) OR (PROSTATE CANCER) OR (PANCREATIC CANCER) O
L18            0 S (L16 OR L17) (P) (L8 OR L14)

=> log y
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                  ENTRY    SESSION
FULL ESTIMATED COST                               88.47      88.68

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)      SINCE FILE      TOTAL
                                                  ENTRY    SESSION
CA SUBSCRIBER PRICE                               -4.34      -4.34

STN INTERNATIONAL LOGOFF AT 09:18:45 ON 17 NOV 2002
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